Accutane (isotretinoin) Questions and Answers

1. Why is FDA taking this action?

FDA has approved a strengthened risk management program called iPLEDGE, to minimize fetal exposure to Accutane (isotretinoin) and its generic equivalents. Isotretinoin is approved for the treatment of the most severe type of acne, severe recalcitrant nodular acne, not responsive to other treatments. Previous programs to reduce the risk of fetal exposure to isotretinoin, the System to Manage Accutane Related Teratogenicity (S.M.A.R.T.) and similar programs from generic drug manufacturers, were assessed in February 2004 by the FDA, and the results of the assessment were presented at a joint meeting of the Drug Safety and Risk Management and Dermatologic and Ophthalmic Drugs Advisory Committees. The joint Advisory Committees recommended strengthening the isotretinoin risk management program to include mandatory registration of all participants and to link negative pregnancy testing to prescription dispensing for female patients who can become pregnant.

2. How is iPLEDGE different from S.M.A.R.T?

Under S.M.A.R.T., isotretinoin was dispensed to patients upon presentation of a written prescription with a yellow adhesive qualification sticker from the prescriber that signified to the pharmacist that the patient was not pregnant. However, sometimes stickers were placed on prescriptions without pregnancy testing being done to ensure that the patient was not pregnant. Under iPLEDGE, wholesalers (including distributors and chain distributors), pharmacies, doctors, and patients must be registered in a computer-based system to control the distribution, prescribing, and dispensing of isotretinoin. A negative pregnancy test must be obtained and confirmed in the system prior to prescription dispensing for female patients who can become pregnant.

3. When will iPLEDGE be implemented?

Starting November 1, 2005

- Only wholesalers registered in iPLEDGE can obtain isotretinoin from manufacturers.
- Only pharmacies registered in iPLEDGE can receive isotretinoin from registered wholesalers.
- Unregistered wholesalers and pharmacies must return unused isotretinoin.

Starting December 31, 2005:

- Only doctors registered in iPLEDGE can prescribe isotretinoin. Doctors registered with iPLEDGE must agree to assume the responsibility for pregnancy counseling of female patients of childbearing potential. Prescribers must obtain and enter into the iPLEDGE system negative test results for those female patients of childbearing potential prior to prescribing isotretinoin

- Only patients registered in iPLEDGE can be prescribed isotretinoin. In addition to registering with iPLEDGE, patients must comply with a number of key requirements that include completing an informed consent form, obtaining counseling about the risks and requirements for safe use of the drug, and, for women of childbearing potential, complying with required pregnancy testing and use of contraception.

4. What must a patient do to get isotretinoin under iPLEDGE?

Patients should discuss isotretinoin and iPLEDGE program requirements with the doctor. Under iPLEDGE each patient must:

- Be registered in iPLEDGE by the doctor prescribing isotretinoin.

- Understand that severe birth defects can occur with the use of isotretinoin by female patients who are or become pregnant.

- Be reliable in understanding and carrying out instructions.

- Read educational materials containing important safety information about isotretinoin and iPLEDGE program requirements.

- Sign a Patient Information/Informed Consent form that contains warnings about the potential risks of taking isotretinoin.

- Fill the prescription within 7 days of the office visit.

- Agree to see the doctor every month during treatment for a progress check-up and to get a new prescription for isotretinoin.

- Not donate or share blood while on isotretinoin and for 1 month after treatment has ended.

- Not share isotretinoin with anyone, even someone who has similar symptoms.

In addition to the requirements for all patients above, female patients who can become pregnant must:

- NOT be pregnant or breast-feeding.

- Have 2 negative pregnancy tests before starting isotretinoin, a negative pregnancy test every month during treatment, and a negative pregnancy test 1 month after treatment has ended.

- Use 2 different forms of birth control at the same time or agree not to have heterosexual intercourse (abstinence) for 1 month before starting isotretinoin, during treatment, and for 1 month after treatment has ended.

- Read educational materials containing important information about pregnancy testing, birth control methods, and actions to take if pregnancy occurs during treatment.

- Sign a second Patient Information/Informed Consent form that contains warnings about the chance of possible birth defects if pregnancy occurs before starting isotretinoin or during treatment.

- Access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) before starting isotretinoin, on a monthly basis during treatment, and 1 month after ending treatment to answer questions about program requirements and to enter two chosen forms of birth control.

5. Were privacy concerns taken into consideration?

Yes. No personal information obtained by doctors about patients will be shared with any outside source. Only information necessary for program goals will be entered into the iPLEDGE system by doctors and patients.

6. How should female patients who can become pregnant who do not have access to the internet or a telephone access the iPLEDGE program monthly?

The iPLEDGE program requires each female patient who can become pregnant to access the iPLEDGE program via the internet or by telephone before starting isotretinoin and monthly during treatment to enter the two chosen forms of birth control and to answer questions on the program requirements.

If a patient does not have access to the internet or to a telephone, she should tell the doctor and ask to make the call from the doctor's office or clinic on the day she sees the doctor.

7. Can pregnancy testing be done using a home pregnancy test?

No. It is important that the most accurate pregnancy tests available be used before starting isotretinoin and during treatment. Except for the first pregnancy test (screening test) obtained by the doctor when the decision is made to pursue qualification of the patient for treatment with isotretinoin, the second pregnancy test (confirmatory test) and all subsequent monthly and post-treatment pregnancy tests must be done in a certified laboratory.

8. Does iPLEDGE make it harder for patients to get isotretinoin?

FDA understands the importance of minimizing any burden imposed upon patients and doctors by iPLEDGE. It is not substantially more difficult for patients to obtain isotretinoin under iPLEDGE than it was for patients who, along with their doctors, were fully compliant with S.M.A.R.T. It is possible that some doctors and pharmacies will choose not to participate in iPLEDGE. A listing of all registered pharmacies will be available via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654).

9. What happens if a pharmacy refuses to dispense isotretinoin to a patient?

There are several reasons why a pharmacy would refuse to dispense isotretinoin to a patient, such as:

- The patient is not registered in iPLEDGE.
- The prescriber is not registered in iPLEDGE.
- The prescription was presented or picked up after the "do not dispense date."
- The pregnancy test results are not in the iPLEDGE system or they are positive.
- The pharmacy is not registered in iPLEDGE.

The patient should talk to the pharmacist or doctor if a pharmacy refuses to dispense isotretinoin for any reason.

If the pharmacy is not registered in iPLEDGE, the patient will be able to access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) for a listing of registered pharmacies.

10. Can patients still get prescriptions filled under S.M.A.R.T.?

Patients who are already being treated with isotretinoin under S.M.A.R.T. (or similar programs) can continue to get their prescriptions filled under those programs until December 30, 2005. To receive treatment with isotretinoin after December 30, 2005, patients must be registered in iPLEDGE.

11. What must a doctor do to register with iPLEDGE?

To register with iPLEDGE, a doctor must:

- Obtain iPLEDGE program information and registration materials via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654).

- Sign and return the completed registration form.

To activate registration, a doctor must access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) and attest to the following points:

- I know how to diagnose and treat acne.

- I know the risk and severity of birth defects from isotretinoin.

- I know the risk factors for unplanned pregnancy and the effective measures for avoidance of unplanned pregnancy.

- I have the expertise to provide the patient with detailed pregnancy prevention counseling or refer her to an expert for such counseling, reimbursed by the manufacturer.

- I will comply with all iPLEDGE program requirements.

- I will counsel female patients who can become pregnant before beginning treatment and on a monthly basis, to avoid pregnancy by using two forms of contraception simultaneously and continuously one month before, during, and one month after isotretinoin therapy unless the patient commits to continuous abstinence.

- I will not prescribe isotretinoin to any female patient who can become pregnant until verifying she has a negative screening pregnancy test and monthly negative CLIA-certified (Clinical Laboratory Improvement Amendment) pregnancy tests.

- I will report any pregnancy case that I become aware of while my female patients are on isotretinoin or one month after the last dose to the pregnancy registry.

12. What must a doctor do to prescribe isotretinoin?

To prescribe isotretinoin, a doctor must:

- Be registered in iPLEDGE (see question #11).

- Access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) to:

  - Register each patient in iPLEDGE.

  - Confirm monthly that each patient has received counseling and education.

  - For female patients who can become pregnant:
    - Enter patient's two chosen forms of contraception each month.
    - Enter monthly result from CLIA-certified laboratory conducted pregnancy test.

13. Can isotretinoin be prescribed for conditions other than severe recalcitrant nodular acne, for example, cystic acne?

Isotretinoin is approved by FDA for the treatment of severe recalcitrant nodular acne. The iPLEDGE program is designed to prevent women who are pregnant or might become pregnant from taking isotretinoin. Because FDA does not regulate the practice of medicine, doctors are not prohibited from prescribing isotretinoin for conditions other than severe recalcitrant nodular acne. However, doctors may only prescribe isotretinoin under iPLEDGE.

14. Does iPLEDGE allow doctors to submit prescriptions by phone, fax, or electronically?

Yes. Doctors may submit prescriptions by phone, fax, or electronically after the initial office visit and subsequent monthly office visits once patient counseling has been provided and the results of pregnancy testing for female patients who can become pregnant are received by the doctor from the lab.

15. Does iPLEDGE allow doctors to delegate required tasks?

Yes. The tasks of obtaining and entering into the iPLEDGE system patient registration information, pregnancy test results, and reported adverse events (including pregnancy exposures) as well as counseling patients and obtaining informed consent may be delegated by doctors to qualified staff.

16. What must a pharmacy do to register in iPLEDGE?

To register in iPLEDGE, a pharmacy must select a Responsible Site Pharmacist who must:

- Obtain iPLEDGE program information and registration materials via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654).

- Sign and return the completed registration form.

To activate registration, the Responsible Site Pharmacist must access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) and attest to the following points:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I will train all pharmacists on the iPLEDGE program requirements.
- I will comply and seek to ensure that all pharmacists comply with iPLEDGE program requirements.
- I will obtain isotretinoin from iPLEDGE registered wholesalers.
- I will return to the manufacturer (or delegate) any unused product.
- I will not fill isotretinoin for any party other than a qualified patient.

To dispense isotretinoin, pharmacists must obtain authorization from iPLEDGE via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) signifying the patient is registered, has received counseling and education, and is not pregnant.

17. What must wholesalers do to register in iPLEDGE?

Wholesalers (including distributors and chain distributors) can obtain iPLEDGE program information and registration materials via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) and must register by signing and returning the wholesaler agreement.

Wholesalers must agree to:

- Distribute only FDA approved isotretinoin.
- Ship isotretinoin only to pharmacies and other wholesalers that are registered in iPLEDGE.
- Notify the manufacturer (or delegate) of any non-registered pharmacy or wholesaler that attempts to order isotretinoin.
- Allow sponsors to assess the wholesalers' compliance with iPLEDGE program requirements.
- Return any undistributed isotretinoin.

- Provide information on how the product is distributed

18. Where can I find more information about iPLEDGE?

Additional information about iPLEDGE may be obtained via the internet (www.ipledgeprogram.com) or by telephone (1-866-495-0654).